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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/259,389	02/26/1999	KATIA GEORGOPOULOS	10287/043001	5245

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EXAMINER	
WOITACH, JOSEPH T	

ART UNIT	PAPER NUMBER
1632	20

DATE MAILED: 06/25/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/259,389	Applicant(s) GEORGOPOULOS ET AL.	
	Examiner Joseph Woitach	Art Unit 1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 April 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5-14,17 and 20-24* is/are pending in the application.

4a) Of the above claim(s) *6-9,12,14 and 17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 5, 10, 11, 13, 20-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☐ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other:

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on April 10, 2002, paper number 17, has been entered.

DETAILED ACTION

This application filed March 26, 1999, claims benefit to provisional application 60/076,325, filed March 27, 1998.

Applicants amendment filed April 10, 2002, paper number 18 has been received and entered. Claims 18 and 19 have been canceled. Claims 1-3, 5, 20 and 21 have been amended. claims 22-24 have been added. Claim

Claims 1-3, 5-14, 17 and 20-24 are pending. Claim 6-9, 12, 14 and 17 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Claims 1-3, 5, 10, 11, 13, and 20-24 are pending and are currently under examination.

Response to Amendment

The declaration of Dr. Katia Georgopoulos under 37 CFR 1.132 filed April 10, 2002, paper number 14, is insufficient to overcome the rejection of the pending claims based upon the rejection made under 35 USC 112, first paragraph, as set forth in the last Office action. It is noted that the declaration is unsigned, however for the sake of compact prosecution the arguments and details presented in the declaration will be discussed as they apply to the instant rejection set forth below.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 20 rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is withdrawn.

Upon review of the portion of the specification pointed to by Applicants, Examiner agrees that the instant specification has literal support for the amendment. Therefore, the new matter rejection is withdrawn.

Claims 1-3, 5, 10, 11 and 13 rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention is withdrawn.

It is noted that the claims have been amended to recite and encompass specific biological activities for the encoded Helios protein. Given a Helios protein with such activities, Examiner would agree that one of skill in the art would be able to use the invention for the further study of the specific activity of the Helios protein in a particular physiological context. Since the product has one enabled use, the requirements for enablement under 35 U.S.C. 112, first paragraph, has been met.

Claims 1, 3, 5, 10, 11, 13, and 20-24 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The final Written Description Examination guidelines that were published on January 5, 2001 (66 FR 1099; available at http://www.uspto.gov/web/menu/current.html).

In the instant case, a nucleic acid sequences encoding a Helios protein other than that set forth in SEQ ID NO: 6 fails to meet written description. It is noted that the claims have been amended to recite specific Helios activities. *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111 (Fed.

Cir. 1991), clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d at 1117. The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed."*Vas-Cath Inc. v. Mahurkar*, 19USPQ2d at 1116. In the instant case, there is adequate written description for any inherent property of the protein for SEQ ID NO: 6, however the specification does not teach how to maintain the inherent properties with any modification to the Helios protein. It is noted that the specification sets forth the particular embodiments recited in the claims, however the specification fails to provide any clear guidance on the specific changes one can make and maintain the recited biological activities. The portions of the specification pointed to by Applicants teaching the similarity of Helios and other family members is noted. However, even in a comparison of conserved and non-conserved amino acids among the various family members, the issue that remains is given any modification of SEQ ID NO: 6 would the artisan readily know if the protein had the activities encompassed by the claim. In the instant case, the skilled artisan is capable of making modifications to polynucleotide sequences which result in altered proteins, however the specification fails to adequately describe what particular modifications one can or can not make. The teaching and comparison with other family members is noted, however the specification does not specifically teach only to modify non-conserved amino acids. Further, given that each of the proteins have shared biological activities,

the uniqueness of each of the family members should come from their differences in amino acid sequence. Besides a general comparison, the specification fails to clearly indicate which amino acids are necessary for any given activity or which ones can be changed without consequence to the activity. As summarized in previous office actions, the application is silent with respect to the role of Helios in any disorder or any examples that point to any specific function of Helios. The art teaches that loss of Ikaros can lead to development disorders, however, this does not clearly support a role for the Helios gene in these disorders. To the contrary, analysis of the expression pattern in different tissues and co-localization of the family members suggests a different role for the Helios gene product. Further, Hahm *et al.* point out that even though work to elucidate the role of Ikaros has been done, 'the specific functions of Helios and of the Helios-Ikaros complex remain unknown' and 'remain to be elucidated' (page 792; discussion). Though further characterization may determine a role of Helios in hematopoietic development, without the detailed experiments performed like those of other Ikaros family members, one can not predict the role or function of Helios. Finally, Kelly *et al.* state [m]utational analysis of the Helios gene will help to dissect its role in regulating progenitor development in the hematopoietic system' (page 514; final paragraph), suggesting the function of Helios is not known, and that one can not relate changes in Helios expression or mutations. In light of the teaching in the present specification the invention encompasses many species of the Helios sequence and fragments thereof which encode functional Helios proteins. They include fragments of Helios, and other variants comprising deletions, substitutions, insertions, additions,

or replacements of Helios sequences. The claimed invention as a whole is not adequately described if the claims require essential or critical elements which are not adequately described in the specification and which are not conventional in the art as of Applicants effective filing date. Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics (as it relates to the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. *Pfaff v. Wells Electronics, Inc.,* 48 USPQ2d 1641, 1646 (1998). In the instant case, the specification provides literal support for the recited embodiments, however the specification fails to describe the relevant identifying characteristics of any of the nucleic acid sequences of any of the sequences which result in a Helios protein with the biological activities recited in the claims besides SEQ ID NO: 6. The portions of the specification pointed to and discussed in the declaration of Dr. Katia Georgopoulos under 37 CFR 1.132 are noted, however these arguments are not persuasive because written description requires more than a mere indication of potential limitations. A comparison of family members may provide the basis for determining conserved sequences, however this does not provide any evidence that they are responsible for any particular biological activity. There is no evidence that these specific conserved amino acid sequences are important to function or whether any alteration will result in a modification of activity. The art of record suggest that loss of Ikaros may result in disorders in a subject, however there is no specific data providing guidance on what amino acids are critical to a particular activity. Even if further

detailed analysis of other family members is known, it is unclear how this would directly correlate to the inherent properties of Helios. While the skilled artisan can envision all the possible variant nucleic acid sequences which would hybridize and encode a variant Helios protein, they do not know which amino acid are critical or which changes will not alter the function of the resulting Helios protein, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method used. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of identifying it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991).

Applicants attention is drawn to the decision of *The Regents of the University of California v. Eli Lilly and Company* (CAFC, July 1997) wherein it was stated:

In claims involving chemical materials, generic formulas usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate written description of the claimed genus. In claims to genetic material, however, a generic statement such as "vertebrate insulin cDNA" or "mammalian cDNA," without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. See *Fiers,* 984 F.2d at 1169-71, 25 USPQ2d at 1605-06 (discussing *Amgen*). It is only a definition of a useful result rather than a definition of what it achieves as a result. Many such genes may achieve that result. The description requirement of the patent statute requires a

description of an invention, not an indication of a result that one might achieve if one made that invention. *See In re Wilder*, 736 F.2d 1516, 222 USPQ 369, 372-373 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.").

Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. In the instant case, Examiner would not contest that some of the variant Helios proteins besides SEQ ID NO: 6 may have the activity recited in the claim and inherent to the Helios protein, however in view of the teachings of the instant specification, the artisan would not know if any given sequence were biological active or maintained the recited functions absent the empirical testing of said variant protein.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence. In the instant case, SEQ ID NO: 6 is the only known protein to meet the biological limitations set forth in the claims, however it is unclear which other variant Helios proteins, and more specifically, what particular alterations can be made to Helios within the full breadth of the claim without empirically testing each variant.

Therefore, only an isolated nucleic acid sequence which encodes a *Helios* protein meet the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3, 5, 10, 11, 13 and 20 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn.

Specifically, the amendments to the claims have obviated the basis of the specific rejections set forth in the previous office action.

Conclusion

No claim is allowed. The claims are free of the art of record because the art fails to teach the polynucleotide sequences which would anticipate the present claims, however the claims are subject to other rejections. Claim 2 is objected to, however would be found allowable if rewritten in independent form encompassing all the embodiments of independent claim 1.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (703)305-3732.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at (703)305-4051.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist Pauline Farrier whose telephone number is (703)305-3550.

Papers related to this application may be submitted by facsimile transmission. Papers should be faxed via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center numbers are (703)308-4242 and (703)305-3014.

Joseph T. Woitach

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